

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
27 October 2005 (27.10.2005)

PCT

(10) International Publication Number  
**WO 2005/100338 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 333/36**,  
409/12, 417/12, A61K 31/381, A61P 35/04

[GB/GB]; 436 Cambridge Science Park, Milton Road,  
Cambridge CB4 0QA (GB).

(21) International Application Number:  
PCT/GB2005/001350

(74) Agents: **HUTCHINS, Michael, Richard** et al.; M.R.  
Hutchins & Co., 23 Mount Sion, Tunbridge Wells, Kent  
TN1 1TZ (GB).

(22) International Filing Date: 13 April 2005 (13.04.2005)

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,  
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/561,600 13 April 2004 (13.04.2004) US  
0408239.2 13 April 2004 (13.04.2004) GB  
60/618,830 14 October 2004 (14.10.2004) US

(71) Applicant (for all designated States except US): **ASTEX  
TECHNOLOGY LIMITED** [GB/GB]; 436 Cambridge  
Science Park, Milton Road, Cambridge CB4 0QA (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GILL, Adrian,  
Liam** [GB/GB]; 436 Cambridge Science Park, Milton  
Road, Cambridge CB4 0QA (GB). **CARR, Maria, Grazia**  
[GB/GB]; 436 Cambridge Science Park, Milton Road,  
Cambridge CB4 0QA (GB). **LYONS, John, Francis**  
[US/GB]; 436 Cambridge Science Park, Milton Road,  
Cambridge CB4 0QA (GB). **THOMPSON, Neil, Thomas**  
[GB/GB]; 436 Cambridge Science Park, Milton Road,  
Cambridge CB4 0QA (GB). **REES, David, Charles**

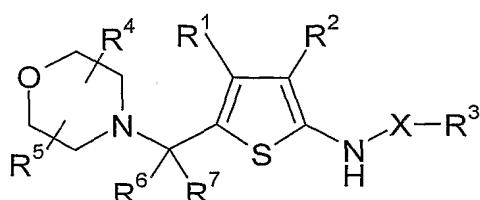
(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 5-MORPHOLINYL METHYL THIOPHENYL PHARMACEUTICAL COMPOUNDS AS P38 MAP KINASE MODULATORS



(I)

(57) Abstract: The invention provides compounds of the formula (I) or a salt, solvate or N-oxide thereof, wherein: R<sup>1</sup> and R<sup>2</sup> are the same or different and each is selected from hydrogen, saturated C<sub>1-3</sub> hydrocarbyl, halogen and cyano; X is selected from C=O, C=S, C(=O)NH, C(=S)NH, C(=O)O, C(=O)S, C(=S)O and C(=S)S; R<sup>3</sup> is selected from aryl and heteroaryl groups each having from 5 to 12 ring members and being unsubstituted or substituted by one or more substituent groups R<sup>10</sup> as defined in the claims; R<sup>4</sup> and R<sup>5</sup> are the same or different and are selected from hydrogen and methyl; or one of R<sup>4</sup> and R<sup>5</sup> is selected from hydroxymethyl and ethyl and the other is hydrogen; and R<sup>6</sup> and R<sup>7</sup> are the same or different and are selected from hydrogen and methyl. The compounds of the formula (I) have activity as p38 MAP kinase and Taf kinase inhibitors.

WO 2005/100338 A1